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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,386	05/03/2007	Stefan Schorling	22398-US	4893

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Patent Law Department
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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
12/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,386	SCHORLING, STEFAN	
	Examiner	Art Unit	
	DAVID C. THOMAS	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed September 22, 2009 is acknowledged. Claims 1, 4, and 7-10 (currently amended) and claims 5, 6, 15 and 16 (original or previously amended) will be examined on the merits. Claims 2, 3 and 11-14 have been newly canceled.

Claim Rejections - 35 USC § 112

2. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 as amended recites the limitation "the second fluorescent label" in claim 9 (ultimately dependent from claim 4). There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1, 4, 5, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schmidt et al., "Parvovirus B19 DNA in plasma pools and plasma

derivatives," Vox Sanguinis, 2001, Vol.81, No.4, pp.228-235 (of record), in view of Hemauer et al., "Sequence variability among different parvovirus B19 isolates," J. General Virology, 1996, Vol.77, pp.1781-1785 (of record), and further in view of Buck et al., "Design Strategies and Performance of Custom DNA Sequencing Primers," Biotechniques, Sept. 1999, Vol.27, No.3, pp. 528-536.

Regarding claim 1, Schmidt discuss a method comprising (a) providing a sample suspected to contain the target nucleic acid, (b) providing a pair of primers comprising a first and a second primer, (c) amplifying the target nucleic acid, and (d) detecting the amplified target nucleic acid of step (c) (see pg.229, "Quantitative TaqMan PCR" where Schmidt discusses the method including two primers and a doubly labeled probe within the NS1 region. Schmidt states the primers and probes are within nucleotides 2030 to 2171 of the B19 Genome).

Regarding claims 4, 5, 8, and 10, Schmidt discusses a method comprising: (a) providing a sample suspected to contain the target nucleic acid, (b) providing a pair of primers comprising a first and a second primer, (c) amplifying the target nucleic acid, (d) contacting the sample with a probe under conditions for binding the probe to the target nucleic acid, and (e) detecting the binding product between the target nucleic acid and the probe as an indication of the presence of the target nucleic acid (see pg.229, "Quantitative TaqMan PCR" where Schmidt discusses the method including two primers and a doubly labeled probe within the NS1 region. Schmidt states the primers and probes are within nucleotides 2030 to 2171 of the B19 Genome).

Regarding claim 9, Schmidt discusses the method wherein the target nucleic acid in step c) is amplified with a template-dependent DNA polymerase (see pg.229, "Quantitative TaqMan PCR" where Schmidt uses TaqGold Polymerase).

Schmidt does not discuss the method whereby the first primer has a nucleic acid sequence SEQ ID NO:15, and whereby the second primer has a nucleic acid sequence SEQ ID NO:17. Schmidt also does not discuss the method wherein the probe has the sequence of SEQ ID NO:11 or a complementary sequence thereof. However, Schmidt discusses primers and a probe that are nearby to such sequences as the instant SEQ ID NOs: 11, 15 and 17 and are located within the same NS1 region of the Parvovirus B19 genome.

Hemauer teaches the Parvovirus B19 DNA, genome position 1924-2317, identified as Genbank Accession Number Z70553. This sequence comprises SEQ ID NO:11 (nucleotides 147-172), SEQ ID NO:15 (nucleotides 121-140) and SEQ I D NO:17 (nucleotides 270-251). In Hemauer's research, he identifies this region (i.e. genome position 1924-2317) being within the NS1 coding region, and is more specifically included in the NS1-C region (see Figure 1). Hemauer also teaches nearby primers to amplify this region (see Table 2 on pg.1783).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers and probe simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for detection of the NS1 region of the Parvovirus B19 genome and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of a polynucleotide sequence, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck

also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to modify the method of Schmidt to use primers of SEQ ID NO:15 and 17 and a probe sequence of SEQ ID NO:11 because Schmidt demonstrates the benefits of designing and using similar primers and a probe targeting the NS1 region of the Parvovirus B19 genome, and Hemauer et al. shows that the Parvovirus B19 sequence comprising the primer sequences of SEQ ID NO:15 and 17 and probe sequences of SEQ ID NO:11 was known in the art and also designed nearby primers that amplify this same region. Additionally, Hemauer also notes that amplification of the NSC-1 region was able to

show positive PCR results in contrast to other regions of the Parvovirus B19 genome and also noted that there is a relatively conserved stretch of about 220 bp with only a few alterations in nucleotides 2020-2240 of this region (see pg.1783, right column). Therefore, since the sequences of primers SEQ ID NO:15 and 17, and probe sequences of SEQ ID NO:11 are located in this conserved stretch, one of skill would have recognized that amplification and detection of such a conserved region would allow for detection of multiple different parvovirus B19 sequences in a universal method. Furthermore, Buck et al. demonstrate the capability of multiple primers to equivalently amplify the same targeted region. Therefore, the skilled artisan would have had a reasonable expectation of success in modifying the method of Schmidt to substitute for similar and equivalent primers and a probe derived from the same well-known and amplifiable conserved stretch of the NSC-1 region, resulting in the predictable amplification and detection of multiple different parvovirus sequence variants. It would have been obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed primer and probe therein.

5. Claims 1, 4-7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harder et al., "New LightCycler PCR for Rapid and Sensitive Quantification of Parvovirus B19 DNA Guides Therapeutic Decision-Making in Relapsing Infections," J. Clin.Microbiol., 2001, Vol.39, No.12, pp.4413-4419 (of record), in view of Hemauer et al., "Sequence variability among different parvovirus B19 isolates," J. General Virology, 1996, Vol.77, pp.1781-1785 (of record), and further in

view of Buck et al., "Design Strategies and Performance of Custom DNA Sequencing Primers," Biotechniques, Sept. 1999, Vol.27, No.3, pp. 528-536.

Regarding claim 1, Harder et al. discuss a method comprising (a) providing a sample suspected to contain the target nucleic acid, (b) providing a pair of primers comprising a first and a second primer, (c) amplifying the target nucleic acid, and (d) detecting the amplified target nucleic acid of step (c) (see pg.4414, "LC-depedent amplification of B19 DNA" where Harder uses NS-1a and NS-1a' as primers and two adjacent donor/acceptor probes in a real-time SYBR green PCR assay).

Regarding claims 4-7, and 10, Harder discusses a method comprising: (a) providing a sample suspected to contain the target nucleic acid, (b) providing a pair of primers comprising a first and a second primer, (c) amplifying the target nucleic acid by contacting the sample with the said pair of primers to produce an amplification product if the target nucleic acid is present in said sample, (d) contacting said sample with the pair of probes, wherein the members of said pair of probes hybridize to said amplification product within no more than five nucleotides of each other, wherein the first probe of said pair of probes is labeled with a donor fluorescent label and wherein the second probe of said pair of probes is labeled with a corresponding acceptor fluorescent label; and (e) detecting the presence or absence of fluorescence resonance energy transfer between said donor fluorescent label of said first probe and said acceptor fluorescent label of said second probe, wherein the presence of fluorescence resonance energy transfer is indicative of the presence of the target nucleic acid in the sample, and wherein the absence of fluorescence resonance energy transfer is indicative of the

absence of the target nucleic acid in the sample (see pg.4414, "LC-depedent amplification of B19 DNA" where Harder uses NS-1a and NS-1a' as primers and two adjacent donor/acceptor probes in a real-time SYBR green PCR assay; and Figures 1 and 2).

Regarding claim 9, Harder discusses the method where amplification is performed using the FastStart SYBR green kit from Roche, which uses a FastStart Taq DNA polymerase that is a modified form of thermostable recombinant Taq DNA polymerase (Taq is a template-dependent DNA polymerase) (see pg.4414, "LC-dependent amplification of B19 DNA").

Harder does not discuss the method whereby the first primer has a nucleic acid sequence SEQ ID NO:15, and whereby the second primer has a nucleic acid sequence SEQ ID NO:17. Harder also does not discuss the method wherein the probe has the sequence of SEQ ID NO: 11. However, Harder teaches primers and probes that are nearby to such sequences as the instant SEQ ID NO: 11, 15 and 17 that are located within the NS1 region of the Parvovirus B19 genome.

Hemauer teaches the Parvovirus B19 DNA, genome position 1924-2317, identified as Genbank Accession Number Z70553. This sequence comprises SEQ ID NO:11 (nucleotides 147-172), SEQ ID NO:15 (nucleotides 121-140) and SEQ I D NO:17 (nucleotides 270-251). In Hemauer's research, he identifies this region (i.e. genome position 1924-2317) being within the NS1 coding region, and is more specifically

included in the NS1-C region (see Figure 1). Hemauer also teaches nearby primers to amplify this region (see Table 2 on pg.1783).

In the court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

Since the claimed primers and probe simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for detection of the NS1 region of the Parvovirus B19 genome and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

With regard to the issue of equivalence of a polynucleotide sequence, MPEP 2144.06 notes "Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is

not necessary to render such substitution obvious. *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982)."

With regard to the issue of reasonable expectation of success in using such equivalents, Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

One of ordinary skill in the art would have been motivated to modify the method of Harder to use primers of SEQ ID NO:15 and 17 and a probe sequence of SEQ ID

NO:11 because Harder demonstrates the benefits of designing and using similar primers and probes targeting the NS1 region of the Parvovirus B19 genome, and Hemauer et al. shows that the Parvovirus B19 sequence comprising the primer sequences of SEQ ID NO:15 and 17 and probe sequences of SEQ ID NO:11 was known in the art and also designed nearby primers that amplify this same region. Additionally, Hemauer also notes that amplification of the NSC-1 region was able to show positive PCR results in contrast to other regions of the Parvovirus B19 genome and also noted that there is a relatively conserved stretch of about 220 bp with only a few alterations in nucleotides 2020-2240 of this region (see pg.1783, right column). Therefore, since the sequences of primers SEQ ID NO:15 and 17, and probe sequences of SEQ ID NO:11 are located in this conserved stretch, one of skill would have recognized that amplification and detection of such a conserved region would allow for detection of multiple different parvovirus B19 sequences in a universal method. Furthermore, Buck et al. demonstrate the capability of multiple primers to equivalently amplify the same targeted region. Therefore, the skilled artisan would have had a reasonable expectation of success in modifying the method of Harder to substitute for similar and equivalent primers and probes derived from the same well-known and amplifiable conserved stretch of the NSC-1 region, resulting in the predictable amplification and detection of multiple different parvovirus sequence variants. It would have been obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods and use the claimed primer and probe sequences therein.

6. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Schmidt et al. (2001), in view of Hemauer et al. (1996), and Buck et al. (1999), as applied to claims 1-5, and 8-14 above, OR Harder et al. (2001), in view of Hemauer et al. (1996), and Buck et al. (1999), as applied to claims 1-7, 9, and 10-14 above and further in view of Andrus et al. (US 7,348,164).

The teachings of the primary references are discussed above. These references do not discuss the method wherein the primer and/ or the probe comprise a modified nucleotide or a non-nucleotide compound.

However, Andrus demonstrates that the use of modified nucleotides or non-nucleotide compounds in primers and probes which detect Parvovirus B19 sequences was conventional in the art at the time of the invention (see abstract, Figures, and col.9, lines 59-67). Therefore, one of skill in the art would have had a reasonable expectation of success in modifying the primer and/or probe of Schmidt, as modified by Hemauer and Buck, or Harder, as modified by Hemauer and Buck, to include a modified nucleotide or a non-nucleotide compound since Andrus demonstrates it was conventional to do in the art at the time of the invention. It would have been *prima facie* obvious to one of skill in the art to carry out the claimed methods and use the claimed primers and/or probe comprising modified nucleotides or a non-nucleotide compounds therein.

7. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Schmidt et al. (2001), in view of Hemauer et al. (1996), and Buck et al. (1999), as

applied to claims 1-5, and 8-14 above, OR Harder et al. (2001), in view of Hemauer et al. (1996), and Buck et al. (1999), as applied to claims 1-7, 9, and 10-14 above, and further in view of Mosquera et al., "Simultaneous Detection of Measles Virus, Rubella Virus, and Parvovirus B19 by Using Multiplex PCR," J. Clin. Micro., 2002, Vol.40, No.1, pp.111-116.

The teachings of the primary references are discussed above. These references do not discuss the method wherein other target nucleic acids are detected in the same reaction.

However, it was conventional in the art to conduct multiplex PCR assays where Parvovirus B19 is detected within the multiplex, as demonstrated by Mosquera et al. Mosquera explains that it is beneficial to detect all three together as the rash illness caused by Rubella Virus, and Parvovirus B19 is easily confused with measles virus infection and differential diagnosis is recommended for surveillance activities (see abstract and pg.11, right column, first full paragraph). Therefore, one of skill in the art would have had a reasonable expectation of success in modifying the method of either one of Schmidt, as modified by Hemauer and Buck, or Harder, as modified by Hemauer and Buck, to detect multiple target nucleic acids with Parvovirus B19 since Mosquera demonstrates that it was conventional in the art to conduct multiplex assays including Parvovirus B19 for the added benefit of being able to distinguish between viral infections which cause similar physical symptoms. It would have been *prima facie* obvious to one of skill in the art to carry out the claimed methods and also detect other target nucleic acids therein.

Response to Arguments

8. Applicant's arguments filed September 22, 2009 have been fully considered but they are not persuasive.

Applicant argues that the claim objections should be withdrawn since the claims have been amended to remove references to non-elected subject matter. The Examiner agrees and the objection is withdrawn.

Applicant then argues that the 35 USC § 112, second paragraph rejection of claims 7 and 10 should be withdrawn since the claims have been amended to correct for improper antecedent basis. The Examiner agrees that with the deletion of the term "hybridizing", claim 7 now has proper antecedent basis and the rejection of claim 7 is withdrawn. However, claim 10 now recites "the second fluorescent label" for which there is insufficient antecedent basis in claims 4, 8 or 9 and therefore the rejection of claim 10 is maintained.

Applicant then argues that the 35 USC § 103(a) rejection of claims 1-3 over Manaresi et al. (U.S. Patent Pub. No. 2003/0099951) in view of Hemauer et al. (J. General Virology, 1996, Vol.77, pp.1781-1785) should be withdrawn based on the following arguments. Applicant argues that while Manaresi teaches general methods for detecting target nucleic acid sequences comprising parvovirus B19, Hemauer does not make up for the deficiency of Manaresi in disclosing all the elements of the claims since Hemauer does not teach a method whereby first and second primers comprise SEQ ID NOs. 15 and 17, respectively. The Examiner agrees that Hemauer fails to

disclose the claimed sequences and that it would not be obvious to use said primers based on the combined teachings of Manaresi and Hemauer. Therefore, the 103(a) rejection of claims 1-3 over Manaresi in view of Hemauer is withdrawn.

Applicant then argues that the 35 USC § 103(a) rejection of claims 1-5 and 8-14 (claims 1, 4, 5 and 8-10 after cancellation of claims 2, 3 and 11-14) over Schmidt et al. (Vox Sanguinis, 2001, Vol.81, No.4, pp.228-235) in view of Hemauer and further in view of Buck et al. (Biotechniques, Sept. 1999, Vol.27, No.3, pp. 528-536) should be withdrawn based on the following arguments. Applicant argues that while Schmidt teaches general methods for detecting target nucleic acid sequences comprising parvovirus B19, Hemauer does not make up for the deficiency of Schmidt in disclosing all the elements of the claims since Hemauer does not teach first and second primers comprising SEQ ID NOs. 15 and 17, respectively, and a probe comprising SEQ ID NO. 11. Applicant further argues that while Hemauer teaches a conserved region (NS1-C) of parvovirus B19 that encompasses the claimed primers and probe sequences, the reference teaches primers that fall outside this region and therefore the claimed primers are not structural homologs of any sequences cited in Hemauer. Applicant argues that the Examiner is basing the equivalency of the primers and probes on the "mere fact that the components at issue are functional or mechanical equivalents", and that even if the primers and probes were functional or mechanical equivalents, the equivalency is not demonstrated by the prior art. The Examiner asserts that equivalency has been recognized in the prior art since the primers and probes of SEQ ID NOs. 11, 15 and 17 are homologous to sequences taught by Hemauer and therefore are structural

homologs of the prior art sequence. Since one of ordinary skill in the art would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are prima facie obvious over the cited reference of Hemauer in the absence of secondary considerations. With regard to secondary considerations, there is no teaching in the claims or specification that the conserved NC1-C region of parvavirus B19 targeted by the claimed primers and probe is unusual in any other way or that using the claimed primers and probes would lead to superior results for detecting parvavirus B19 relative to using other primers and probes.

Applicant further argues that the teachings of Buck in which large numbers of control primers are used to amplify a different target indicating a reasonable expectation of success for every primer is irrelevant to amplification of an unrelated target such as NS1-C of parvovirus B19, and that is had been well established that primers in different regions do not function equivalently. Applicant reiterates that Hemauer does not teach any primers within the conserved NS1-C region and that the Examiner has not demonstrated any primer equeivalent in Buck, Hemauer or Schmidt. As discussed above, equivalency has been established since the prior art teaches homologs of the claimed primers and probes. Furthermore, Hemauer does teach the use of primers within the NS1-C region for amplification of sequences shared by NS1-C and the adjacent delta V region (Hemauer, primers deltaV F1, nt 2193-2209, and deltaV F2, nt 2229-2245, Table 2). Moreover, Schmidt teaches amplification using TP1 and TP2 primers within the NS1-C region to produce a 142-base pair amplicon between nucleotides 2030 and 2171 (p. 229, column 2, lines 31-42). This region overlaps

substantially with the region amplified by the claimed primers (nucleotides 2044-2193), with primers TP1 and SEQ ID NO. 15 overlapping six nucleotides. Therefore, it is obvious that this region can be successfully amplified and detected using other primers and probes, and that the claimed primers are not functionally superior to others cited in the prior art. Therefore, based on all the discussions above, the 103(a) rejection of claims 1, 4, 5 and 8-10 over Schmidt in view of Hemauer and further in view of Buck is maintained.

Similarly, the 103(a) rejection of claims 1, 4-7, 9 and 10 over Harder et al. (J. Clin.Microbiol., 2001, Vol.39, No.12, pp.4413-4419) in view of Hemauer and further in view of Buck is maintained since it has been concluded that equivalency has been established, as the prior art of Hemauer teaches homologs of the claimed primers and probes that is further supported by Buck, while Harder teaches methods of amplifying parvavirus B19 NS1 sequences in a real-time SYBR green PCR assay.

Similarly, the 103(a) rejection of claim 15 over Schmidt in view of Hemauer and Buck, or Harder in view of Hemauer and Buck, and further in view of Andrus (U.S. Patent No. 7,348,164) is maintained since it has been concluded that equivalency has been established, as the prior art of Hemauer teaches homologs of the claimed primers and probes that is further supported by Buck, while Schmidt and Harder each teach methods of amplifying parvavirus B19 NS1 sequences in a real-time PCR assay, and furthermore, the limitations taught by Andrus are not argued separately.

Finally, the 103(a) rejection of claim 16 over Schmidt in view of Hemauer and Buck, or Harder in view of Hemauer and Buck, and further in view of Mosquera (J. Clin.

Micro., 2002, Vol.40, No.1, pp.111-116) is maintained since it has been concluded that equivalency has been established, as the prior art of Hemauer teaches homologs of the claimed primers and probes that is further supported by Buck, while Schmidt and Harder each teach methods of amplifying parvavirus B19 NS1 sequences in a real-time PCR assay, and furthermore, the limitations taught by Mosquera are not argued separately.

Summary

9. Claims 1, 4-10, 15 and 16 are rejected. No claims are free of the prior art.

Conclusion

10. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David C Thomas/
Examiner, Art Unit 1637

/Kenneth R Horlick/
Primary Examiner, Art Unit 1637